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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/284,155	07/14/99	LOFFLER	WWH-188

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EXAMINER
FORMAN, B

ART UNIT	PAPER NUMBER
1655	

DATE MAILED: 10/14/99

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

**Office Action Summary**

Application N .

09/284,155

Applicant(s)

LOFFLER ET AL.

Examiner

BJ Forman

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☒ received.
2. ☐ received in Application No. (Series Code / Serial Number) \_\_\_\_.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

- 14) ☒ Notice of References Cited (PTO-892)
- 15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1.
- 17) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 18) ☐ Notice of Informal Patent Application (PTO-152)
- 19) ☐ Other: \_\_\_\_\_.

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## **DETAILED ACTION**

### ***Specification/Informalities***

The disclosure is objected to because of the following informalities:

References to sequences are not in proper format according to 37 CFR 1.821.

Reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:".

The abstract of the disclosure is objected to because of a typographical error in line 8 that recites "PCR rejection". Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-14 are rejected because Claim 1 is drawn to a method, but the claim lacks a step that accomplishes the goal of the method. Specifically, a method for detecting resistant fungal cells must detect resistant fungal cells. It is suggested the

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claims be amended to include "wherein detection of the hybridized probes detects azole derivative-resistant cells".

Claims 15-22 are rejected because "from the enclosed sequence listing" is not proper claim language. It is suggested that the claims be amended because in a printed patent, the sequence listing is part of the patent and not an enclosure.

Claims 24-26 are indefinite because it is unclear what "as in" Claim 4(claims 24 & 23) or Claim 1 (Claim 26) means. It is unclear whether "as in" means the method of Claim 4 (1) or an unrecited similar method.

Claim 25 is indefinite because it is unclear what the kit contains. Additionally, applicant is reminded that a proper Markush Group (see Ex parte Markush, 1925 C.D. 126 (Comm'r Pat.1925) recites members as being "selected from the group consisting of A, B, and C. It is suggested that applicant amend the claim to read, SEQ ID NO: 7 and SEQ ID NO: 8.

Claim 26 is rejected because it is missing the kit elements and/or it lacks proper antecedent basis because Claim 1 does not recite components of a kit.

Claims 23 & 24 are drawn to the use of nucleotide sequences in a composition, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

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Claims 23 & 24 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966). For the purpose of searching the prior art, Claims 23 & 24 are considered compositions.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 & 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Geber *et al.* (Antimicrob. Agents Chemo. 1995 39(12) 2708-2717). The claims of the instant application are drawn to a method for detecting resistant fungal cells wherein the method steps of Claim 1 are drawn to extraction of fungal-specific nucleic acids, and hybridization of the extracted nucleic acids with probes directed against nucleic acid segments of azole derivative-resistant fungal cells. Claim 2 depends from Claim 1 wherein the probes are directed against a DNA segment from the 14- $\alpha$ -lanosterol

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demethylase gene. Claim 4 depends from Claim 2 wherein the 14- $\alpha$ -lanosterol demethylase gene is amplified by PCR before hybridization with 14- $\alpha$ -lanosterol demethylase gene-specific probes.

Geber *et.al.* disclose a method to detect fungal species resistant to azole anti-fungal agents. Their method of detection consists of: a) extraction of nucleic acids from fungal cells, b) amplification of the azole-derivative resistance 14- $\alpha$ -lanosterol demethylase gene using gene-specific primers and PCR (page 2709), and c) hybridization of the extracted nucleic acids with probes directed against a DNA segment from the 14- $\alpha$ -lanosterol demethylase gene (page 2714).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 11 & 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Geber *et.al.* (Antimicrob. Agents Chemo. 1995 39(12) 2708-2717) as applied to claims 1, 2 & 4 above, and further in view of Lai & Kirsch (Nuc. Acids Res. 1989 17(2) 804).

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The embodiments of Claims 3, 5, 11 & 26 of the instant application differ from Geber *et al.* wherein:

The 14- $\alpha$ -lanosterol demethylase gene from the species *Candida albicans* is identified by hybridization using sequence-specific probes (Claim 3), a PCR reaction is performed in which segments of the *C. albicans* 14- $\alpha$ -lanosterol demethylase gene are amplified and the amplified products are hybridized with probes directed against the 14- $\alpha$ -lanosterol demethylase gene (Claim 5), and probes are labeled with digoxigenin and used in Southern hybridization (Claim 11).

However, Geber *et al.* disclose labeled probes used for Southern hybridization (page 2714) and PCR amplification of the 14- $\alpha$ -lanosterol demethylase gene (page 2709). Digoxigenin labeled probes were known in the art at the time the invention was made (Jordan U.S. Patent No. 5,426,026, 20 June 1995 ) and the skilled practitioner absent any unexpected results would have known to select digoxigenin or any other label based on experimental requirements and/or expected results.

Additionally, the the *C. albicans* 14- $\alpha$ -lanosterol demethylase gene sequence was known in the art at the time the invention was made as taught by Lai & Kirsch.

It would have been ***prima facie*** obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Geber *et al.* with the teachings of Lai *et al.* to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the Geber *et al.* method for detecting azole-derivative resistant *Candida glabrata* to the

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closely related *C. albicans* because the latter, like *C. glabrata* was a known clinical pathogen, “the major fungal pathogen of humans” (Lai *et al.*), known to be resistant to azole-derivative anti-fungal agents (Geber *et al.*, page 2708, second paragraph), and known to share 65% homology in the *C. albicans* 14- $\alpha$ -lanosterol demethylase derived amino acid sequence (Geber *et al.*, page 2712, second column). In particular, the skilled artisan would have been motivated to perform PCR amplification followed by probe detection as in Geber *et al.* by the prior art availability of the *C. albicans* 14- $\alpha$ -lanosterol demethylase gene sequence (Lai *et al.*) for selecting primer and probe sequences modeled after those of Geber *et al.*

The further embodiment of a kit for performing the method of Claim 1 (Claim 26). would have been known to one of ordinary skill in the art at the time the invention was made because kits were known in the art (see Jordan, Claims 10-12). It would have been ***prima facie*** obvious to one of skill in the art to combine the components taught by Geber *et al.* in a kit for detecting resistant fungal cells because the skilled practitioner would have been motivated with a reasonable expectation of success by the expected benefits of the experimental predictability and commercial benefits to assemble the components for detecting azole-resistant fungal cells in a kit.

### ***Conclusion***

Claims 6-10, 12-15 & 25 are free of the prior art and can be placed in condition for allowance by resolution of the rejections stated above.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703)306-5878. The examiner can normally be reached on 7:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703)308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)308-8742 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

BJ Forman, Ph.D.  
October 7, 1999

*S. Forman*  
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